IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner Lyle A. Alexander
ART UNIT 1743

In re application of
E. Alan Bates et al.
Application No. 08/935,629
Filed 09/23/97
For ASSAYING DEVICE ....

DECLARATION UNDER 37 CFR 1.132

Commissioner for Patents
Washington, DC 20231

I, Gary Hoffman, declare as follows:

1. I am the third joint inventor for this application.

2. While the claims of this application have been rejected based on the patent of Senior, the disclosure of the application starts from a technology actually quite different from that of Senior. Characteristic of this difference is Senior's provision of its bibulous member 16 protruding out of the housing. When the bibulous member is placed in a urine stream, it is quickly soaked. Senior has correctly chosen to display this version in its drawings, because versions such as suggested in paragraph a. in col. 5 of Senior would tend to shield the bibulous member from a urine stream.

3. This application references in its BACKGROUND a quite different technology, that of drug testing using an immunoassay method called antigen-antibody competitive binding. Characteristic of this technology is the measured application of only a few drops of urine. This dropwise application of the urine is disclosed in the specification in the first paragraph of the DETAILED DESCRIPTION OF THE INVENTION.

4. Attached hereto are Exhibits 1 to 5 demonstrating five different instances of the type

of technology forming the starting point for this application. These are as follows:

Exhibit 1 - Pages 1-4 of a document entitled "AccuSign DOA 4, THC/OPI/COC/AMP" bearing copyright notice dated 1996;

Exhibit 2 - Pages 1-4 of a document entitled "AccuSign BAR", also bearing copyright notice dated 1996;

Exhibit 3 - Front and back of a leaflet headed "Drug Test Resources International", likewise concerning AccuSign DOA 4 and bearing a 1996 copyright notice;

Exhibit 4 - One-sided, undated leaflet headed "Visaline II"; and

Exhibit 5 - Copies of the packages of several kits labeled HOME DRUG TEST and their instruction leaflets.

5. Exhibit 1 is noteworthy for the correspondence of the terminology in its section Principle on its page 1 with the terminology in the BACKGROUND section of this application.

6. All of the exhibits direct that 3 drops of urine be applied, this being a standard for this techology. All of the exhibits provide either a dropper or a pipette for transfer of the urine sample into the sample well. In each of the exhibits, the sample receiving area is clearly a well, and Exhibit 1, for instance, calls it a "well" in the section Test Protocol on its page 2.

7. The chart at the top of page 2 of Exhibit 1, for instance, explains that appearance of a line for a particular drug in this starting technology is a negative indication, i.e. the drug is not present in amounts above the cutoff level.

8. A characteristic of this technology is that the sample collection location must not be flooded with urine, as in Senior, because this leads to false positives hy washing out the lines that would otherwise indicate negative readings.

9. It is to be noted that none of these exhibits mentions photocopying the results. The statements regarding photocopying in the BACKGROUND section of the present application represent perceptions of the present inventor group, rather than the state of the art at the time this invention was made.

10. While the provision of a cap to cover Senior's wet, protruding member 16 is immediately understandable, it was the present group of inventors which perceived the advantages of such for the different technology from which the present invention arose.

11. A difference between the present invention and Senior concerns the problem with putting a cap on Senior's test. Because the bibulous material can be so flexible (especially when wet) there often is difficulty slipping the cap on without bending the material. It's like threading a needle by holding the thread still and moving the needle

12. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; such statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and may jeopardize the validity of the application or any patent issued thereon.

Signature: Gary A. Date: 8-21-00

AccuSign™ *DOA 4*

THC/OPI/COC/AMP

One-Step Panel Assay for Drugs of Abuse

For *In Vitro* Use Only

Simple One-Step Immunoassay for the Qualitative Detection of THC metabolites, Opiates, Cocaine metabolite, Amphetamines, and/or their Metabolites in Urine

PBM

Catalog No	DOA-240	35 Test Kit
	DOA-240-10	10 Test Kit

Intended Use

The **AccuSign™** ***DOA 4 THC/OPI/COC/AMP*** Panel Assay is a simple, one-step immunochromatographic test for the rapid, qualitative detection of THC metabolites, opiates, cocaine metabolite, and amphetamines in urine. The test detects the major metabolites of these drugs at the following cutoff concentrations.

THC	11-nor-Δ⁹-THC-9-carboxylic acid	50 ng/mL
OPI	Morphine	300 ng/mL
COC	Benzoylecgonine	300 ng/mL
AMP	Amphetamine	1000 ng/mL

The* AccuSign™ *DOA 4 THC/OPI/COC/AMP test provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography, mass spectrometry (GC/MS) is the preferred confirmatory method. Other chemical confirmatory methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.[1]

Summary and Explanation

Drug abuse has become one of the most destructive social problems in recent years, affecting nearly every corner of the world. To effectively combat this increasingly disturbing problem, there is a strong need for a simple, rapid, inexpensive, disposable, visual, and non-instrument requiring drug screening test kit. According to the National Institute on Drug Abuse (NIDA), THC (Marijuana), Opiates, Cocaine, and Amphetamines are among the most widely abused drugs. The one-step **AccuSign™** ***DOA 4*** Panel Assay is a test for screening these four major drugs of abuse in urine, simultaneously with one sample application. The test takes less than 10 minutes to perform.

THC (Δ⁹-tetrahydrocannabinol) is the primary active ingredient in cannabinoids (marijuana). When ingested or smoked, it produces euphoric effects. Users experience impairment of short term memory and THC use slows learning. Also, it may cause transient episodes of confusion, anxiety, or frank toxic delirium. Long term, relatively heavy use may be associated with behavioral disorders. The peak effect of smoking THC occurs in 20–30 minutes and the duration is 90–120 minutes after one cigarette. Elevated levels of urinary metabolites are found within hours of exposure and remain detectable for 3–10 days after smoking. The main metabolite excreted in the urine is 11-nor-Δ⁹-tetrahydrocannabinol-9-carboxylic acid.

Opioid analgesics comprise a large group of substances which control pain by depressing the central nervous system. Morphine is the prototype compound of this group.[2] Morphine is excreted unmetabolized, and is also the major metabolic product of codeine and heroin. Morphine is detectable in the urine for several days after an opiate dose.

Cocaine, derived from the leaves of coca plant, is a potent central nervous system (CNS) stimulant and a local anesthetic. Cocaine induces euphoria, confidence and a sense of increased energy in the user; these psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine is used by smoking, intravenous, intranasal or oral administration, and excreted in the urine primarily as benzoylecgonine in a short time. Benzoylecgonine has a longer biological half-life (5–8 hours) than cocaine (0.5–1.5 hours) and can generally be detected for 24–60 hours after cocaine use or exposure.[3,4]

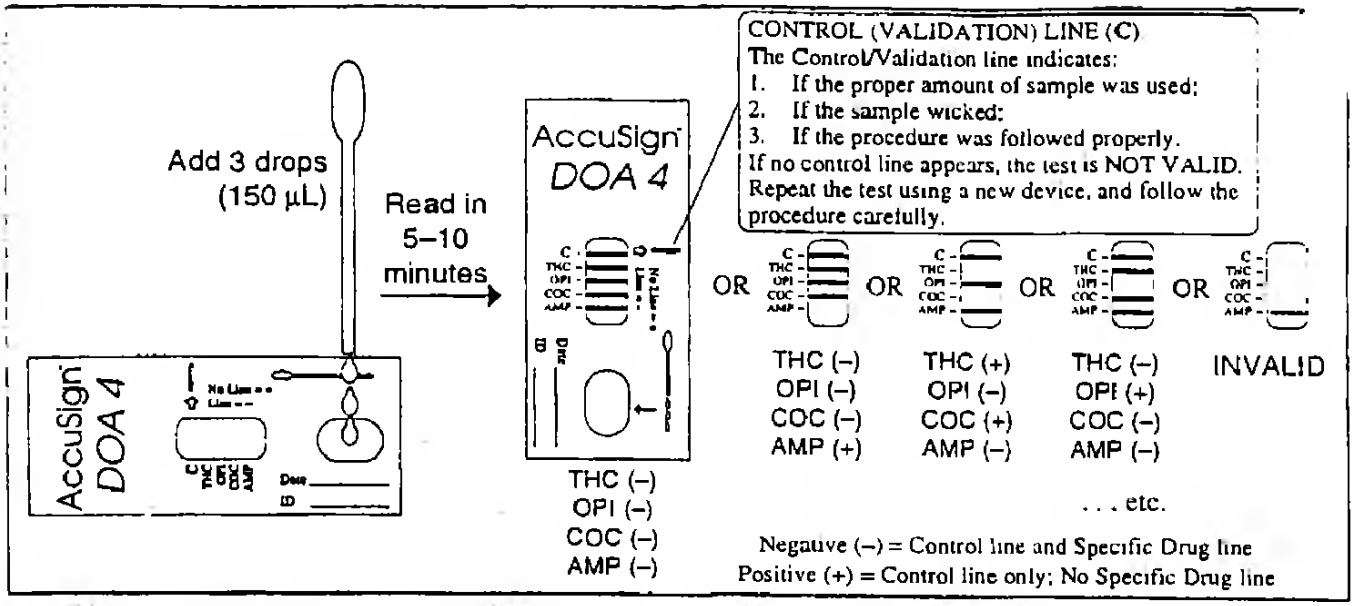
Amphetamine is a potent sympathomimetic agent with therapeutic applications. The drug can be taken orally, injected, or inhaled. Acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power.[3] Cardiovascular responses to amphetamine include increased blood pressure and cardiac arrhythmias. More acute responses include anxiety, paranoia, hallucinations, psychotic behavior, and eventually, depression and exhaustion. The effects of amphetamine generally last 2–4 hours, and the drug has a half-life of 9–24 hours in the body. Amphetamine is excreted in the urine in unchanged form and also as hydroxylated and deaminated derivatives.[4]

Principle

The **AccuSign™** ***DOA 4*** test employs one-step, solid-phase immunoassay technology to discretely detect the presence of any of the above four drugs, or their immunoreactive metabolites, in urine. The assay uses highly specific monoclonal/polyclonal antibodies raised against the target drugs. The test card contains a membrane strip, on which each of the four drugs conjugated to BSA is immobilized at specific locations. The assay is based on the principle of the highly specific immunochemical reactions between antigens and antibodies which are used for the analysis of specific substances in biological fluids. The drug detection relies on the competition for binding to the antibodies between drug conjugates and drugs which may be present in the urine sample.

In the test procedure, a sample of urine is placed in the sample well of the device, and the sample is allowed to migrate upward. If any of the four drugs is present in the urine sample, it forms a complex with the antibody-dye conjugate specific for that drug, and the complex migrates toward the opposite end of the card, passing the specific locations on the membrane where each of the four drug conjugates is immobilized. The drug in the sample competes with the drug conjugate, which is immobilized on the membrane, for the limited antibodies present in the form of antibody-dye conjugate. When a sufficient amount of drug is present, the drug will saturate the antibodies, and the antibody-dye conjugate cannot bind to the drug conjugate on the membrane. Therefore, a drug-positive urine sample will not generate a line at the specific drug position in the result window, indicating a positive result from positive drug competition. Conversely, if a particular drug is absent in the urine specimen, the antibody on the antibody-dye conjugate will bind the membrane-bound drug. In this case, a drug-negative urine sample will generate a line at the specific drug position in the result window, indicating a negative result from an absence of competition with free drug.

EXHIBIT 1



In addition, the test card has a procedural control built into the system, in the upper control line area. The control line is immobilized with polyclonal anti-mouse antibody; therefore, it will capture monoclonal antibody-dye conjugates that pass the region, showing a colored line in the control (validation) zone. The line works as a procedural control, confirming that proper sample volume was used and the reagent system worked. If insufficient sample volume is used, there may not be a control line, indicating the test is invalid.

Materials Provided

The AccuSign™ *DOA 4* test kit contains all the reagents necessary to perform the assay.

- AccuSign™ *DOA 4* device. The test device contains a membrane coated with drug conjugates in a protein matrix and a pad containing mouse monoclonal anti-THC antibody–dye conjugate, mouse monoclonal anti-opiate antibody-dye conjugate, mouse monoclonal anti-benzoylecgonine antibody–dye conjugate, and polyclonal sheep anti-amphetamine antibody-dye conjugate in a protein matrix.
- Disposable sample dispenser.
- Instructions for use.

Precautions

- For *in vitro* diagnostic use only.
- Avoid cross contamination of urine samples by using a new urine specimen container and dropper for each urine sample.
- This test kit does not contain any HIV or hepatitis infective components. However, urine specimens are potentially infectious. Proper handling and disposal methods should be followed, according to good laboratory practices.
- The AccuSign™ device should remain in its original sealed pouch until ready for use.
- Do not use the test kit after the expiration date.

Storage and Stability

The AccuSign™ *DOA 4* test kit should be stored at 2–30°C (35–86°F) in the original sealed pouch. The expiration dating was established under these storage conditions.

Specimen Collection and Preparation

Approximately 150 µL of urine sample is required for each test. Fresh urine specimens do not require any special handling or pretreatment. Specimens should be collected in a clean glass or plastic container. If testing will not be performed immediately, specimens should be refrigerated (2–8°C) or frozen. Specimens should be brought to room temperature before testing.

Specimens containing a large amount of particulate matter may give inconsistent test results. These specimens should be clarified by centrifuging or allowing to settle before testing.

Test Procedure

The test procedure consists of adding the urine sample to the Sample well of the device and watching for the appearance of colored lines in the result window.

Test Protocol

1. For each test, open one AccuSign™ *DOA 4* pouch and label the AccuSign™ device with the patient ID.
2. Holding the dropper vertically, dispense 3 full drops (150 µL) of the urine sample into the Sample well.
3. Read the result after 5–10 minutes.

Interpretation of Results

Negative: The appearance of a reddish-purple Control line (C) and a line for a specific drug indicates a negative test result; i.e., no drug above the cutoff level has been detected. The color intensities of the Control line and specific drug line may not be equal. *A negative test result does not indicate the absence of drug in the sample, it indicates only that the sample does not contain drug above the cutoff level in qualitative terms.*

Positive: The appearance of only a reddish-purple Control line and no distinct line next to a specific drug name indicates the test result is positive for that drug (i.e., the specimen contains the drug at a concentration above the cutoff level). *A positive test result does not provide any indication of the level of intoxication or urinary concentration of the drug in the sample; it indicates only that the sample contains drug above the cutoff level in qualitative terms.*

Invalid: A distinct Control line (C) should always appear. The test is invalid if no Control line forms at the C position. Such tests should be repeated with a new AccuSign™ *DOA 4* test device.

Examples of possible results are shown in the diagram above.

THC (–), Opiates (–), Cocaine (–), Amphetamines (–): Five reddish-purple lines—one Control line at the **C** position and one each at the **THC**, **OPI**, **COC**, and **AMP** positions.

- **THC (–), Opiates (–), Cocaine (–), Amphetamines (+):** Four reddish-purple lines—one Control line at the **C** position and one line each at the **THC**, **OPI**, and **COC** positions; no line at the **AMP** position.
- **THC (+), Opiates (–), Cocaine (+), Amphetamines (–):** Three reddish-purple lines - one Control line at the **C** position, one line each at the **OPI** and **AMP** positions; no lines at the **THC** and **COC** positions.
- **THC (–), Opiates (+), Cocaine (–), Amphetamines (–):** Four reddish-purple lines—one Control line at the **C** position and one line each at the **THC**, **COC**, and **AMP** positions; no line at the **OPI** position.
- There are other possible results, depending on the combinations of drugs present in the urine sample.

Note: A very faint line for a specific drug in the result window, visible in 10 minutes, indicates that the amount of drug in the sample is near or below the cutoff level of the test. These urine specimens must be retested, or confirmed with a more specific alternative method such as gas chromatography/mass spectrometry, before positive determinations are made.

Limitations

- The test is designed for use with unadulterated urine only.
- There is a possibility that factors such as technical or procedural errors, as well as other substances in the urine sample than those listed in Table 4 below, may interfere with the test and cause erroneous results.
- Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results regardless of the method of analysis. If adulteration is suspected, the test should be repeated with a new sample.
- This test detects only the presence of THC metabolites, opiates, cocaine metabolite, amphetamines, and/or their metabolites in urine. A positive test result does not provide any indication of the level of intoxication or urinary concentration.
- The test result read after 10 minutes may not be consistent with the original reading obtained within the 10 minute reading period. The test result must be read within 10 minutes of sample application.
- Certain medications containing opiates or opiate derivatives, amphetamines, or methamphetamines may produce a positive result in any chemical or immunological assay. Additionally, foods and tea containing poppy products and/or coca leaves may produce a positive result. Prolonged passive smoking of THC may also produce a positive result.

User Quality Control

Quality Control. Control standards are not supplied with this kit; however, it is recommended that a control be tested as good laboratory testing practice. NIDA recommends that positive quality control specimens be at or near the cutoff concentration. For information on how to obtain controls, contact PBM's Technical Services. Before using a new kit with patient specimens, positive and negative controls should be tested to confirm the test procedure, and to verify the tests produce the expected Q.C. results. Q.C. specimens should also be run anytime there is any question concerning the validity of results obtained.

Process Control. The Control line can be considered an internal process control. A distinct reddish-purple Control line should always appear if the test procedure is performed properly, an adequate sample volume is used, the sample and reagent are wicking on the membrane, and the test reagents are working. If the Control line does not appear in the control or validation line area, the test is invalid and a new test should be performed. If the problem persists, contact PBM for technical assistance.

Expected Values

AccuSign™ *DOA 4* is a qualitative assay. The amount of drugs and metabolites present in urine cannot be estimated by the assay. The assay results distinguish positive from negative samples. Positive results indicate the samples contain the specific drug above the cutoff concentration.

Performance Characteristics

The **AccuSign™ *DOA 4*** Panel Assay detects THC, opiates, cocaine, amphetamines, and their metabolites at cutoff levels based on the recommendations of the National Institute on Drug Abuse (NIDA) for screening of these drugs in urine.[1,2,3,4]

THC	11-nor-Δ^9-THC-9-carboxylic acid	50 ng/mL
OPI	Morphine	300 ng/mL
COC	Benzoylecgonine	300 ng/mL
AMP	D-Amphetamine	1000 ng/mL

The accuracy of **AccuSign™ *DOA 4*** was evaluated in comparison to a commercially available immunoassay (Syva® EMIT® II) for each of these four drugs. About 1000 random clinical samples for each drug, including at least 250 positive samples above the cutoff level for each of the four drugs, was tested by both procedures, using the cutoff values listed. Complete agreement was observed in > 99% of the samples as shown below. (Table 1.)

Table 1. Accuracy: Comparison of AccuSign™ *DOA 4* with Syva® EMIT® II Assay

		Syva® EMIT® II (THC)		
		Positive	Negative	TOTAL
AccuSign™ DOA 4 (THC)	Positive	305	5	310
	Negative	11	680	691
TOTAL		316	685	1001

		Syva® EMIT® II (OPI)		
		Positive	Negative	TOTAL
AccuSign™ DOA 4 (OPI)	Positive	249	0	249
	Negative	1	716	717
TOTAL		250	716	966

		Syva® EMIT® II (COC)		
		Positive	Negative	TOTAL
AccuSign™ DOA 4 (COC)	Positive	362	1	363
	Negative	14	644	658
TOTAL		376	645	1021

		Syva® EMIT® II (AMP/MET)		
		Positive	Negative	TOTAL
AccuSign™ DOA 4 (AMP)	Positive	185	0	185
	Negative	4	291	295
TOTAL		189	291	480

	Relative Sensitivity	Relative Specificity
THC	96.5% (305/316)	99.2% (680/685)
Opiates	99.6% (249/250)	> 99% (716/716)
Cocaine	96.3% (362/376)	99.8% (644/645)
Amphetamine	97.8% (185/189)	> 99% (291/291)

In a separate study, **AccuSign™ *DOA 4*** was evaluated against specimens confirmed as positive by GC/MS, for each of the four drugs. The results below demonstrate the excellent correlation of **AccuSign™ *DOA 4*** with GC/MS (99% agreement). (Table 2.)

Table 2. Accuracy: Comparison of AccuSign™ *DOA 4* with GC/MS Assay

		AccuSign™	GC/MS
THC	Positive	87	88
	Negative	1	0
OPI	Positive	73	74
	Negative	1	0
COC	Positive	77	78
	Negative	1	0
AMP	Positive	55	56
	Negative	1	0

Precision and Accuracy

The precision of the AccuSign™ *DOA 4* Panel Assay was determined by carrying out the test with serially diluted standard drug solutions. About 98% of the samples containing cocaine, opiates, or amphetamine and about 90% of the samples containing THC concentrations 25% over the cutoff level consistently showed positive results.

The study also included over 40 samples ± 25% cutoff level as a challenge of cutoff precision. These results were found to be consistently in agreement with expected test results.

Distribution of Random Error:

Twenty (20) blind samples prepared by spiking various concentrations of cocaine, THC, morphine, or amphetamine were separately tested by two operators. The test results from the two operators showed complete agreement.

Reproducibility

The reproducibility of the test results of the AccuSign™ *DOA 4* Panel Assay was examined at three different sites using a total of 15 blind controls, consisting of 5 negative samples, 5 moderately positive samples, and 5 strongly positive samples (i.e., a concentration 3 times the cutoff level). The results obtained at these three sites with these controls demonstrated 100% agreement with each other.

Specificity

The following table lists compounds that are detected by the AccuSign™ *DOA 4* test. The specificity of the AccuSign™ *DOA 4* test was determined by adding various drugs and drug metabolites to drug-negative urine specimens and testing with the AccuSign™ *DOA 4* test kit. The results are expressed in terms of the concentration required to produce a positive result. (Table 3.)

Table 3. Specificity

Compound	Concentration (ng/mL)	% Cross-reactivity
THC		
Cannabinol	15,000	0.3
11-nor-Δ⁸-THC-9-COOH	30	160
11-nor-Δ⁹-THC-9-COOH	50	100
Δ⁸-THC	25,000	0.2
Δ⁹-THC	10,000	0.5
OPI		
Codeine	300	100
Glucuronide	300	100
Hydrocodone	500	60
Hydromorphone	600	50
Levophanol	5,000	6
Meperidine	80,000	0.4
Morphine	300	100
Morphine-3-β-D-glucuronide	500	60
Nalorphine	1,000	30
Naloxone	100,000	0.3
Norcodeine	60,000	0.5
Oxycodone	20,000	1.5
Oxymorphone	60,000	0.5
Procaine HCl	100,000	0.3
Thebaine	5,000	6
COC		
Benzoylecgonine	300	100
Cocaine HCl	500	60
Ecgonine HCl	1,000	30
AMP		
D-Amphetamine	1,000	100
L-Amphetamine	7,000	14
D,L-Amphetamine sulfate	1,000	100
p-OH-Methamphetamine	30,000	3.3
Methylenedioxyamphetamine	500	200
Methylenedioxymethamphetamine	10,000	10
β-Phenethylamine	20,000	5
Phentermine	5,000	20
Tryptamine	100,000	1
3-OH-Tyramine	90,000	1.1

The following compounds show no cross-reactivity when tested with AccuSign™ *DOA 4* at a concentration of 100 µg/mL. (Table 4.)

Table 4. Non Cross-Reacting Compounds

Acetaminophen	Dextropropoxyphene	Naproxen
Acetylsalicylate	Diazepam	Norethindrone
Aminopyrine	Diphenylhydantoin	Penicillin
Amitriptyline	Epinephrine	Pentobarbital
Amobarbital	Erythromycin	Phencyclidine
Amoxapine	Estriol	Phenolbutazone
Ampicillin	Gentisic acid	Phenylpropanol-amine
Apomorphine	Glutethimide	Prednisone
Ascorbic acid	Guaiacol glycerol ether	Secobarbital
Atropine	Hydrochlorothiazide	Tetracycline
Benzocaine	Imipramine	Tetrahydrozoline
Butabarbital	Lidocaine	Trifluoperazine
Chlordiazepoxide	Methadone	Tryptamine
Chlorphentramine	Methaqualone	Zomepirac
Chlorpromazine	Methyprylon	
Chloroquine		

References

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6. Blum K. *Handbook of Abusable Drugs*. 1st ed. New York. Gardner Press, Inc., 1984.

PBM
Princeton BioMeditech Corporation
P.O. Box 7139, Princeton, New Jersey 08543-7139 U.S.A.
4242 U.S. Route 1, Monmouth Junction, New Jersey 08852-1905 U.S.A.
Tel: (908) 274–1000
Fax: (908) 274–1010

AccuSign™ BAR

New One-Step Barbiturates Test

For *In Vitro* Forensic Use Only

Simple One-Step Immunoassay for the Qualitative Detection of Barbiturates in Urine

PBM

Catalog No. DOA-206 35 Test Kit
DOA-206-10 10 Test Kit

Intended Use

The AccuSign™ BAR test is a simple, one step, immunochromatographic assay for the rapid, qualitative detection of barbiturates in urine with a cutoff at 300 ng/mL for secobarbital.

The AccuSign™ BAR test provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography, mass spectrometry (GC/MS) is the preferred confirmatory method. Other chemical confirmatory methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

Summary and Principle of Procedure

Barbiturates are a group of chemicals derived from barbituric acid. Classified as hypnotics, they depress the central nervous system. Taken orally in pill or tablet form, they are prescribed by many medical conditions, usually for their sedative effect. Abuse of barbiturates can, however, lead not only to impaired motor coordination and mental disorder, but also to respiratory collapse, coma and death. The combination of barbiturates and alcohol is particularly dangerous.

Symptoms of barbiturate abuse include drowsiness, slurred speech and irritability. Acute conditions include respiratory collapse and loss of consciousness. Chronic conditions include addiction, abstinence, seizures and death. The effects last 3 to 6 hours (30 to 20 hours for phenobarbital). Barbiturates minimally remain detectable in urine for 4 to 6 days (3 weeks for phenobarbital).

Principle

The AccuSign™ BAR test uses solid phase immunoassay technology for the qualitative detection of secobarbital and barbiturate metabolites in human urine. The test is based on the principle of the highly specific immunochemical reactions between antigens and antibodies which are used for the analysis of specific substances in biological fluids. The test relies on the competition for binding to the antibodies between drug conjugates and drug in which may be present in the urine sample. In the test procedure, a sample of urine is placed in the sample well of the device and is allowed to migrate upward. If drug is present in the urine sample it competes with the drug conjugate, which is immobilized on the membrane, for the limited antibodies present in the form of dye-antibody conjugate. When a sufficient amount of drug or drug metabolite above the cutoff level is present, the drug will saturate the antibodies, thus inhibiting the binding of dye-antibody conjugate to the drug conjugate on the membrane. This prevents the formation of a line on the membrane. Therefore, a drug positive urine sample will not generate a line in the test window, indicating a positive result from positive drug competition, while a negative urine sample will generate a line in the test window, indicating a negative result from an absence or competition with free drug.

In addition to the Test line that may appear in the Test window (T), a control line is present in the Control window (C) to confirm the viability of the test. This Control should always be seen, if the test is conducted properly. It works as a procedural control, confirming that proper urine volume was used and the reagent system worked. If insufficient sample volume is used, there may not be a Control line indicating the test is invalid.

Materials Provided

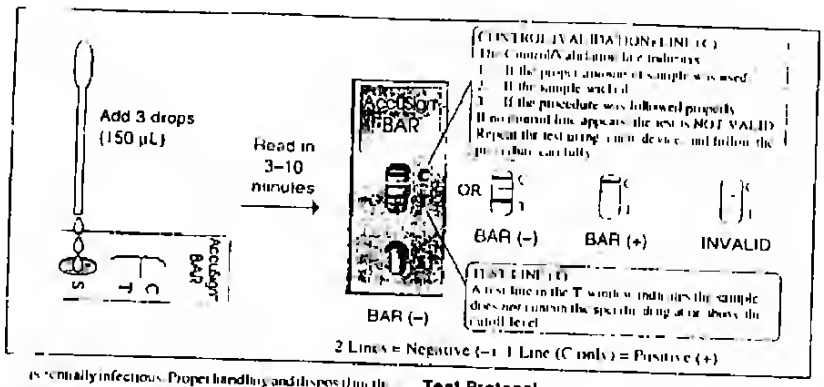
The AccuSign™ BAR test kit contains all the test components necessary to perform the assay:

- AccuSign™ BAR device: The test device contains a membrane coated with drug conjugate and a pad containing polyclonal anti-barbiturate antibody dye conjugate in a protein matrix.
- Disposable sample dispenser
- Instructions for use

Precautions

- For *in vitro* forensic use only.
- Avoid cross-contamination of urine samples by using a new sample dispenser for each urine sample.
- This test kit does not contain any HIV or hepatitis infectious components. However, urine specimens

EXHIBIT 2



is potentially infectious. Proper handling and disposal methods should be followed according to good laboratory practices.

- The AccuSign™ device should remain in its original sealed pouch until ready for use.
- Do not use the test kit after the expiration date.

Storage and Stability

The AccuSign™ BAR test kit should be stored at 2–30°C (36–86°F) in the original sealed pouch. The expiration date was established under these storage conditions.

Specimen Collection and Preparation

Approximately 150 µL of urine sample is required for each test. Fresh urine specimens do not require any special handling or pretreatment. Specimens should be collected in a clean glass or plastic container. If testing will not be performed immediately, specimens should be refrigerated (2–8°C). Store frozen. Specimens should be brought to room temperature before testing.

Specimens containing a large amount of particulate matter may give inconsistent test results. Such specimens should be clarified by centrifuging or allowing to settle before testing.

Test Procedure

The test procedure consists of adding the urine sample to the sample well of the device and watching for the appearance of colored lines in the result window.

Test Protocol

1. For each test, open one AccuSign™ BAR pouch and label the AccuSign™ device with the patient ID.
2. Holding the dropper vertically, dispense 3 drops (150 µL) of the urine sample into the Sample well (S).
3. Read the result after 3 minutes, but within 10 minutes of sample addition.

Interpretation of Results

Negative: Two Lines. The appearance of two reddish-purple lines—one in the Test window (T) and the other in the Control window (C)—indicates a negative test result, i.e., no barbiturates above the cutoff level have been detected. The color intensity of the Test line may be weaker or stronger than that of the Control line. *A negative test result does not necessarily indicate the absence of drug in the sample; it only indicates the sample does not contain drug above the cutoff level in qualitative terms.*

Positive: One Line. The appearance of only one reddish-purple line in the Control window (C) and no distinct line in the Test window (T) indicates the test result is positive, i.e., the specimen contains barbiturates at a concentration above the cutoff level. *A positive test result does not provide any indication of the level of intoxication or urinary concentration of the drug in the sample; it only indicates the sample contains drug above the cutoff level in qualitative terms.*

Invalid: A distinct colored line should always appear in the Control window (C). The test is invalid if no line forms in the Control window (C). Such tests should be repeated with a new AccuSign™ BAR test device.

Note: A very faint line in the Test window (T) visible in 10 minutes, indicates that the amount of barbiturates in the sample is near or below the cutoff level of the test. These urine specimens must be retested or confirmed with a more specific alternative method such as gas chromatography/mass spectrometry before positive determinations are made.

Limitations

- The test is designed for use with unadulterated urine only.
- There is a possibility that factors such as technical or procedural errors as well as other substances in the urine sample which are not listed in Tables 2 or 3 below may interfere with the test and cause erroneous results.
- Adulterants, such as bleach and/or alum in urine specimens may produce erroneous results regardless of the method of analysis. If adulteration is suspected the test should be repeated with a new sample.
- This test detects only the presence of barbiturates and/or their derivatives in urine. A positive test result does not provide any indication of the level of [illegible] or urinary concentration.
- The test result read after 10 minutes may not be consistent with the original reading obtained within the 10 minute reading period. The test must be read within 10 minutes of sample application.
- Certain medications containing barbiturates may produce a positive result in any chemical or immunological assay.

User Quality Control

Quality Control: Control standards are not supplied with this kit; however, it is recommended that a control be tested as good laboratory testing practice. NIDA recommends that positive quality control specimen be at or near the cutoff concentration. For information on how to obtain controls, contact PBM's Technical Services. Before using a new kit with patient specimens, positive and negative controls should be tested to confirm the test procedure and to verify the tests produce the expected Q.C. results. Q.C. specimens should also be run anytime there is any question concerning the validity of results obtained.

Process Control: The Control line can be considered an internal process control. A distinct reddish-purple Control line should always appear if the test procedure is performed properly, an adequate sample volume is used, the sample and reagent are wicking on the membrane, and the test reagents are working. If the Control line does not appear in the control or validation line area, the test is invalid and a new test should be performed. If the problem persists, contact PBM for technical assistance.

Expected Values

AccuSign™ BAR is a qualitative assay. The amount of secobarbital or barbiturate metabolites present in the urine cannot be estimated by the assay. The assay results distinguish positive from negative samples. Positive results indicate the samples contain barbiturates above the cutoff concentration.

Performance Characteristics

The AccuSign™ BAR test has been shown to detect an average of 300 ng/ml of secobarbital in urine. The test also detects other barbiturates listed below at the minimum concentrations indicated (Table 2).

The accuracy of AccuSign™ BAR was evaluated in comparison to a commercially available immunoassay (Syva® EMIT® II). A total of 302 samples was tested by both procedures. The overall accuracy of the test was 98.7%, as shown below (Table 1.)

Table 1. Accuracy Comparison of AccuSign™ BAR with Syva® EMIT® II

		Syva® EMIT® II (BAR) Positive	Negative	TOTAL
AccuSign™ BAR	Positive	105	0	105
	Negative	4	193	197
TOTAL		109	193	302

	Relative Sensitivity	Relative Specificity
AccuSign™ BAR	96.3% (105/109)	> 99.9% (193/193)

Precision and Accuracy

The precision of AccuSign™ BAR was determined by carrying out the test with serially diluted standard drug solutions. About 98% of the samples containing drug levels 25% over the cutoff level consistently showed positive results.

The study also included over 40 samples ± 25% cutoff level as a challenge of cutoff precision. These results were found to be consistently in agreement with expected test results.

Distribution of Random Error:

Twenty (20) blind samples prepared by spiking various concentrations of drug were separately tested by two operators. The test results from the two operators showed complete agreement.

Reproducibility

The reproducibility of the test results of AccuSign™ BAR was examined at three different sites using a total of 15 blind controls, consisting of 5 negative samples, 5 moderately positive samples, and 5 strongly positive samples (i.e., [illegible] concentration 3 times the cutoff level). The results obtained at these three sites with these controls demonstrated 100% agreement with each other.

Specificity

Compounds that are detected by the AccuSign™ BAR test are listed below (Table 2). The specificity of AccuSign™ BAR was determined by adding various drugs and drug metabolites to drug-negative urine specimens and testing with the AccuSign™ BAR test kit. The results are expressed in terms of the concentration required to produce a positive result.

Table 2. *Specificity*

Compound	Concentration (ng/mL)	% Cross-reactivity
Allobarbital	200	150
Alphenal	1,000	30
Amobarbital	2,000	15
Aprobarbital	200	150
Barbital	2,000	15
Butabarbital	500	60
Butalbital	200	150
Cyclopentobarbital	500	60
Pentobarbital	1,000	30
Phenobarbital	5,000	6
Secobarbital	300	100

The following compounds show no cross reactivity when tested with AccuSign™ BAR at a concentration of 100 μg/ml (Table 3).

Table 3. Non Cross-Reacting Compounds

4-Acetamidophenol
Acetophenetidin (Phenacetin)
N-Acetylprocainamide
Acetylsalicylic acid
Aminopyrine
Amitriptyline
Amoxapine
Amoxicillin
D,L-Amphetamine
L-Amphetamine
Apomorphine
Aspartame
Atropine
Benzilic Acid
Benzoic acid
Benzoylecgonine
Benzphetamine
Cannabinol
Chloral hydrate
Chloramphenicol
Chlordiazepoxide
Chlorothiazide
Chlorpromazine
Chloroquine
Cholesterol
Clomipramine
Clonidine
Cocaine
Codeine
Cortisone
(-)-Cotinine
Creatinine
Deoxycorticosterone
Dextromethorphan
Diazepam
Diclofenac
Diethylpropion
Diflunisal
Digoxin
Diphenhydramine
[illegible]
Doxylamine
Ecgonine
Ecgonine methylester
(-)-Ephedrine
(±)-Ephedrine
(+)-Ephedrine
(-)-Ψ-Ephedrine
Erythromycin
β-Estradiol
Estrone-3-sulfate
Ethyl-p-aminobenzoate
Fenoprofen
Furosemide
Gentisic acid
Glucuronide
Glutethimide
Guaifenesin
Hippuric acid
Hydralazine
Hydrochlorothiazide
Hydrocodone
Hydrocortisone
Hydromorphone
O-Hydroxyhippuric acid
3-Hydroxytyramine
Ibuprofen
Imipramine
Iproniazid
(-)-Isoproterenol
Isoxsuprine
Ketamine
Ketoprofen
Labetalol
Levorphanol
Lidocaine
Loperamide
Loxapine succinate
Maprotiline
Meperidine
Meprobamate
Methadone
p-Hydroxymethamphetamine
Methaqualone
Methoxyphenamine
(±) 3,4-Methylenedioxyamphetamine
(±) 3,4-Methylenedioxymethamphetamine
Methylphenidate
Methyprylon
Morphine-3-β-D-glucuronide
Nalidixic acid
Nalorphine
Naloxone
Naltrexone
Naproxen
Niacinamide
Nifedipine
Norcodein
Norethindrone
Noroxymorphone
D-Norpropoxyphene
(-)-Norpseudoephedrine
Noscapine
Nylidrin
D,L-Octopamine
Oxalic acid
Oxazepam
Oxolinic Acid
Oxycodone
Oxymetazoline
Oxymorphone
Papaverine
Penicillin-G
Pentazocine
[illegible]
Perphenazine
Phencyclidine
Phendimetrazine
Phenelzine
Pheniramine
Phenol
L-Phenylephrine
β-Phenylethylamine
Phenylpropanolamine
Prednisolone
Prednisone
Procaine
Promazine
Promethazine
D,L-Propranolol
[illegible]
D-Propoxyphene
D-Pseudoephedrine
Quinidine
Quinine
Ranitidine
Salicylic acid
Secobarbital
Serotonin
Sulfamethazine
Sulindac
Temazepam
Tetracycline
Tetrahydrocortisone
Tetrahydrozoline
Thebaine
Thiamine
Thioridazine
D,L-Thyroxine
Tolbutamide
Triamterene
Trifluoperazine
Trimethoprim
Trimipramine
Tryptamine
D,L-Tryptophan
Tyramine
D,L-Tyrosine
Uric acid
Verapamil
Zomepirac

References

1. Hawks RL, Chiang CN, eds. *Urine Testing for Drugs of Abuse*. Rockville, MD: National Institute on Drug Abuse (NIDA), Research Monograph 73; 1986.
2. Baselt RC. *Disposition of Toxic Drugs and Chemicals in Man*. 2nd Ed., Davis, CA: Biomedical Publ.; 1982: p.488.

PBM
Princeton BioMeditech Corporation
P.O. Box 7139, Princeton, New Jersey 08543-7139 U.S.A.
4242 U.S. Route 1, Monmouth Junction, New Jersey 08852-1905 U.S.A.
Tel: (908) 274-1000
Fax: (908) 274-1010

DRUGTEST℠
RESOURCES INTERNATIONAL

Presents the AccuSign™ DOA Series

One-Step Drug Test with Results in Only 2-5 Minutes

- Easy to Read Color
- Highly Sensitive
- Built-In Test Control
- No Refrigeration
- Eliminates Timing
- Simultaneous Testing Capability of Multi-Drugs

Tests are available in single or multiple test panels for the following drugs:

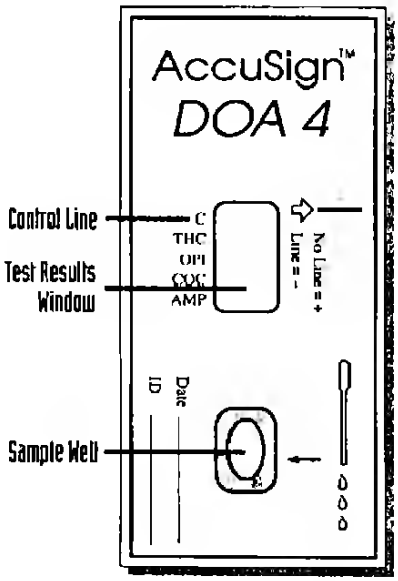
Amphetamines	Cocaine	PCP
Barbiturates	Methamphetamines	THC (Marijuana)
Benzodiazepines	Morphine/Opiates	

Watch us for More Tests & New Technology

EXHIBIT 3

AccuSign™ DOA Series

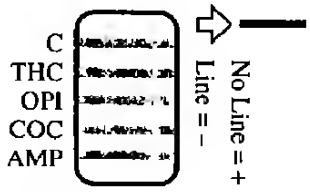
Test Procedure



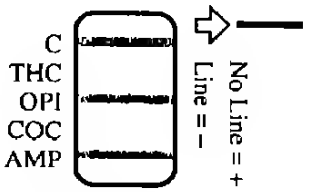
1. Using the plastic pipette, add 3 drops of urine sample to the Sample Well.
2. Read results in 2 to 5 minutes (within 10 minutes).
3. Interpret Test Results Window:
   - CONTROL LINE - A colored line indicates the test is complete and the system has worked properly.
   - NEGATIVE - A colored line for the specific drug indicates the test is negative and the drug was NOT DETECTED.
   - POSITIVE - No colored line for the specific drug indicates the test is positive and the drug was DETECTED.

Tests Manufactured by Princeton BioMeditech Corporation

Samples



THC (-) negative
Opiates (-) negative
Cocaine (-) negative
Amphetamines (-) negative



THC (+) positive
Opiates (-) negative
Cocaine (+) positive
Amphetamines (-) negative

For information or to place an order call:

UNIVERSAL DRUG TESTING
476 ROUTE 61
LARGE, PA 18625

Visualine™ II

One Step Drug Screening Test

AVITAR TECHNOLOGIES, INC. produces, markets and distributes medical devices for the health care industry.

Avitar now distributes rapid Tests for Drug Abuse that are:

- accurate
- sensitive
- simple to use

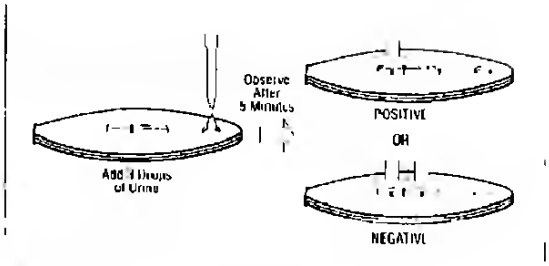
The Visualine™ II tests[1] which have FDA approval to market are:

- Cocaine
- Morphine
- Cannabinoids (THC)
- Benzodiazepines

The tests are composed of preformulated dry reagents arranged on a porous membrane support in a convenient cassette. To perform the tests, just add a few drops of urine to the sample well of the device and wait five minutes. Results are then easily read in the results window as the presence or absence of a red line. A built in reference control ensures that the sample has been added and that the test is effective. The tests are based on the newest lateral flow micro-particle immunoassay technology and have been evaluated in clinical trials at a major university. The Visualine™ II tests are designed to meet NIDA proposed cutoff levels.

[1] A test for Methamphetamine is available for uses that do not require FDA approval to market

Visualine™ II test device and pipette.



Simple to use and simple to read.

For information contact customer service at
1.800.255.0511

AVITAR TECHNOLOGIES, INC.
65 Dan Road, Canton, Massachusetts 02021

EXHIBIT 4

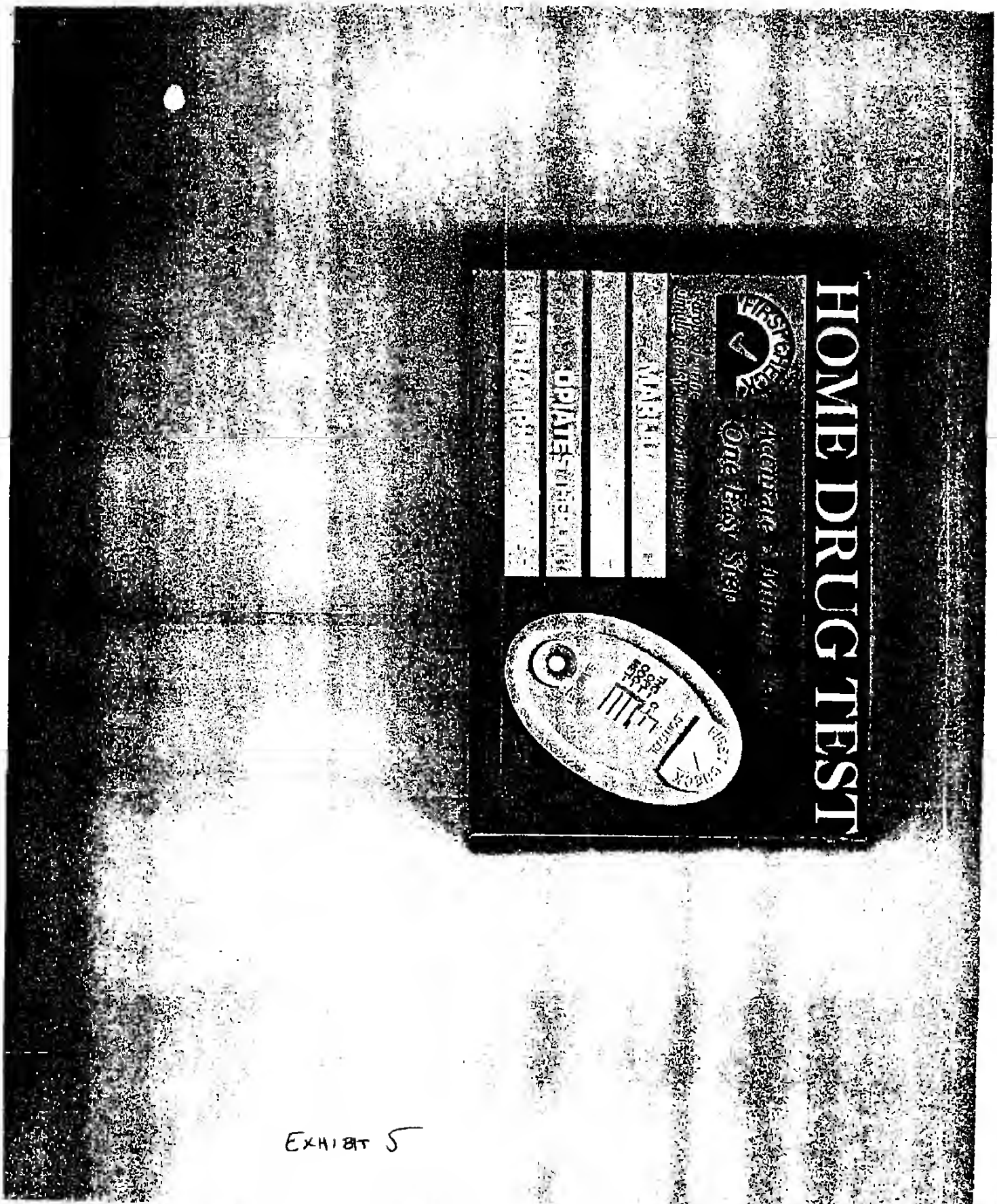


EXHIBIT 5

For information about other home drug tests call 888-788-5716.
Worldwide Medical Corporation, Irvine, CA 92618 • http://www.wwmed.com

EASY TO TEST

- *Add 3 drops of urine*
- *Wait 5 minutes*
- *Read results*

EASY TO READ RESULTS

control line
THC
OPI
COC
MET
negative
positive

First Check® provides immediate information about the use of marijuana, cocaine, opiates and methamphetamines. It is not for legal, law enforcement, or medical purposes. For diagnosis and treatment, consult with health care or substance abuse professional.

This box contains:
1 test well
1 sample dispenser
Instructions

Material required but not provided:
Clean glass or plastic container for collection of sample.

6 43281 06905 4

For external use only. Store at 40-86°F (4-30°C). Read enclosed directions completely before use

Current Drug Usage Trends
Marijuana use increased 43% in junior high (grades 6-8) and 28% in high school students (grades 9-12).
National Parents' Resource Institute for Drug Education, Inc. (PRIDE 9th annual students' survey (September 25, 1996)

In 1995, cocaine related episodes comprised 27% of all emergency department drug related episodes.
1995 Preliminary Estimates of Drug-Related Emergency Department Episodes. SAMHSA/OAS (August, 1996)

The potency of marijuana has doubled since the 1970s.
"Marijuana Potency Monitoring Project: Quarterly Report", 1996. Mississippi: University of Mississippi, Research Institute of Pharmaceutical Sciences

Methamphetamine-related emergency department episodes rose 256% between 1991 and 1994.
1995 Preliminary Estimates of Drug-Related Emergency Department Episodes. SAMHSA/OAS (August, 1996)

Among emergency room cocaine-related episodes, "dependence" was the most commonly reported motive for drug use in 1995.
1995 Preliminary Estimates of Drug-Related Emergency Department Episodes. SAMHSA/OAS (August, 1996)

In 1994, when manner of drug abuse death was accidental, cocaine was mentioned in 55% and heroin/morphine in 53% of medical examiner cases.
Statistical Series, Series I, Number 14-B, Drug Abuse Warning Network (DAWN), U.S. Dept. of Health and Human Services

A higher prevalence of depression, motivational problems, and interpersonal problems are associated with marijuana use.
Conn Foundation, Marijuana and Today's Youth (1997)

Educational Materials

Growing Up Drug Free: A Parent's Guide to Prevention. *U.S. Department of Education, Washington, D.C., NCADI Publication No. PHD533, 1993*

Keeping Youth Drug Free: A Guide for Parents, Grandparents, and Other Caregivers. *Center for Substance Abuse Prevention, U.S. Department of Health and Human Services, 1995*

Marijuana: Facts for Teens. *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD713, 1995*

Marijuana: Facts Parents Need to Know. *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD712, 1995*

Support Groups

Al-Anon Family Group Headquarters
P.O. Box 862
Midtown Station
New York, NY 10018-0862
800/344-2666

World Service Office, Inc.
P.O. Box 9999
Van Nuys, CA 91409
818/773-9999

Marijuana Anonymous
World Services Office
P.O. Box 2912
Van Nuys, CA 91404
800/766-6779

Families Anonymous, Inc.
P.O. Box 3475
Culver City, CA 90231-3475
800/736-9805

WORLDWIDE MEDICAL
CORPORATION
Irvine, CA 92618 USA
Toll-free 888/788-4316
Visit Worldwide Medical Corporation at http://www.wwmed.com

Commonly Asked Questions:

Q: [illegible]

A: No. The lines need not be the same shade or intensity. The control line may look darker than a test line, or vice versa.

Q: How long will the colored line remain visible?

A: The test should be read within 10 minutes for best results. A negative result (5 lines, 1 line in Control window and 4 lines in Test window) will never disappear.

Q: I am not sure of my test result. What should I do?

A: The test is working properly as long as a colored line is visible in the Control window. The result is negative for marijuana, morphine/opiates, cocaine, and methamphetamines if there are also 4 lines in the Test window. The result is positive if there is no line next to a drug name in the Test window.

Q: Do I have to wait the full 5 minutes before reading the test?

A: Yes, we recommend that you wait the full 5 minutes before reading the result. However, if your test clearly shows negative (5 lines, a line in the Control window and 4 lines in the test window), you do not need to wait. If a line in the test window is not clear, your result will be more accurate after 5 minutes. Most negative test results will be clearly readable in 1 minute. To be sure of a positive (1 line in Control window and no line next to a drug name in the Test window), wait 5 minutes but no longer than 10 minutes.

Q: What if my child refuses to give a urine sample?

A: Patiently gain your child's cooperation with the understanding that it is their welfare that you are protecting. Should your child question the importance of testing him or her for drugs or the seriousness of occasional drug usage, page 4 of this pamphlet supplies current data on drug usage among our youth and why you, as a parent, cannot ignore this possibility. Be persistent without accusations, threats, or anger. If your child continues to refuse, seek professional help. Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information and educational resources for more information.

Q: Even though the result is negative, I still feel that my child may be using drugs. What can I do?

A: Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information.

Q: Even though the result is positive, my child claims to be not using drugs. What can I do?

A: Save the unused portion of the urine sample. Ask your family physician for a recommended laboratory to retest the same sample

HOME DRUG TEST

Instructions for Use

First Check®
Marijuana (THC), Morphine/Opiates, Cocaine, & Methamphetamines

When the need to know is....now

- **Simple - one step**
- **Easy-to read**
- **Confidential**
- **Result in 5 minutes**

First Check® Marijuana, Morphine/Opiates, Cocaine, & Methamphetamines provides immediate information about the use of marijuana, morphine/opiates, cocaine, and methamphetamines. It is not for legal law enforcement or medical purposes. For diagnosis and treatment, consult with a healthcare or substance abuse professional.

Read the following directions completely before use.

For external use only.
Store at 40-86°F (4-30°C).

FOR EDUCATIONAL USE ONLY

First Check® is a registered trademark of Worldwide Medical Corporation

First Check®

Not to be taken internally.

Marijuana (THC), Morphine/Opiates, Cocaine, & Methamphetamines

Marijuana

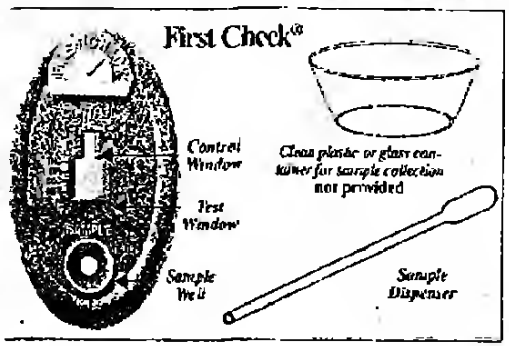
THC is the primary active ingredient in marijuana (cannabinoids). When ingested or smoked, it produces euphoric efforts. Users have impairment of short term memory and marijuana use slows learning. Also, it may cause transient episodes of confusion, anxiety, or even frank toxic delirium. Long term, relatively heavy use may be associated with behavioral disorders. The peak effect of smoking marijuana occurs in 20-30 minutes and the duration is 90-120 minutes after one cigarette. Elevated levels of urinary metabolites are found within hours of exposure, and remain detectable for 3-10 days after smoking.

Morphine/Opiates

Opioid analgesics comprise a large group of substances which control pain by depressing the central nervous system. Morphine is the prototype compound of this group. Up to 15% of the morphine dose is eliminated in the urine as glucuronide. Free morphine in the urine accounts for about 10% of the dose, while very small amounts of morphine-6-glucuronide and morphine-3-ethereal sulfate are also present. Approximately 5% of a dose of morphine is N-demethylated to normorphine which is found as a urinary metabolite in both the free (1%) and conjugated (4%) forms. Codeine is excreted as glucuronide conjugate, as free and conjugated norcodeine, and as morphine. Morphine is detectable in the urine for several days after an opiate dose. Heroin is a semisynthetic derivative of morphine.

Cocaine

Cocaine, derived from the leaves of the coca plant, is a potent central nervous system (CNS) stimulant and a local anesthetic. Cocaine induces euphoria, confidence and a sense of increased energy in the user; these psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine is used by smoking, intravenous, intranasal or oral administration. Cocaine base can be smoked in a form that is commonly known as "crack" which is especially likely to lead to dependence because of its more rapid and heightened effect on the abuser. Cocaine is eliminated in the urine primarily as unchanged drug (1-9%, dependent on urine pH), benzoylecgonine (35-54%), and ecgonine (not quantitated) in a 24 hour period and excreted in the urine primarily as benzoylecgonine in a short time. Benzoylecgonine has a longer biological half-life (5-8 hours) than cocaine (0.5-1.5 hours) and can generally be detected for 24-60 hours after cocaine use or exposure.



Methamphetamines

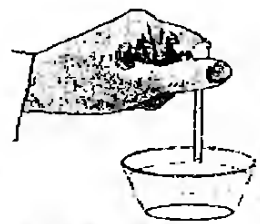
Methamphetamine is a potent sympathomimetic agent with therapeutic applications. The drug can be taken orally, injected, or inhaled. Acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power. Cardiovascular responses to methamphetamine include increased blood pressure and cardiac arrhythmias. More acute responses include anxiety, paranoia, hallucinations, psychotic behavior, and eventually, depression and exhaustion. The effects of methamphetamine generally last 2-4 hours, and the drug has a half-life of 9-24 hours in the body. Methamphetamine is excreted in the urine primarily as amphetamine and oxidized and deaminated derivatives. However, 10-20% of methamphetamine is excreted unchanged. Thus the presence of the parent compound in the urine indicates methamphetamine use. Methamphetamine is generally detectable in the urine for 3-5 days, depending on urine pH level.

Before you begin

Read all the information in this pamphlet before performing the test. First, make sure you are familiar with the test kit contents shown below. Store at 36-86° F (2-30° C) in the sealed pouch, away from direct sunlight. Do not use after the expiration date stamped on the package.

Instructions

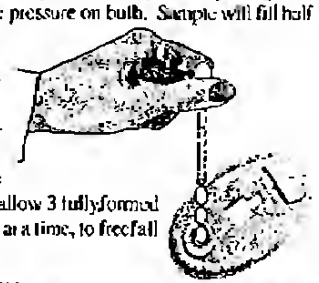
1. Open the sealed pouch, remove the First Check® card, and set the card on a flat surface with Test and Control windows facing up.



2. Collect urine sample in a clean plastic or glass container.

Do not discard the unused urine until after the test has been completed and the result interpreted.

3. With sample dispenser over sample, press bulb between thumb and index finger, insert dispenser opening into sample and release pressure on bulb. Sample will fill half of dispenser tube.



4. With sample dispenser in vertical position over Sample well of test card, gently squeeze dispenser bulb, to allow 3 fully formed drops of urine, one at a time, to freefall into Sample well.

Do not add more than 3 drops of sample into the well. Adding additional drops may cause inaccurate results.

5. Allow the test card to remain undisturbed until result is read. Read the result after 5 minutes but within 10 minutes.

Results

Wait at least 5 minutes but not more than 10 minutes before reading result.

Negative

Five horizontal lines, one line in the Control (upper) window and four line in the Test (lower) window, mean there is no marijuana, morphine/opiates, cocaine, nor methamphetamine present in the urine sample. *The line in the Test window may be lighter or darker than the line in the Control window.*

no drug taken

Positive

One line in the Control window and no line next to a drug name in the Test window means the sample contains that drug.

drug taken (cocaine)

Invalid Test

A distinct colored line should always appear in the Control (upper) window. If no line appears in the Control window, do not interpret result.

Limitations

The First Check® One-Step Home Drug Test is not reusable. The test instructions must be followed precisely.

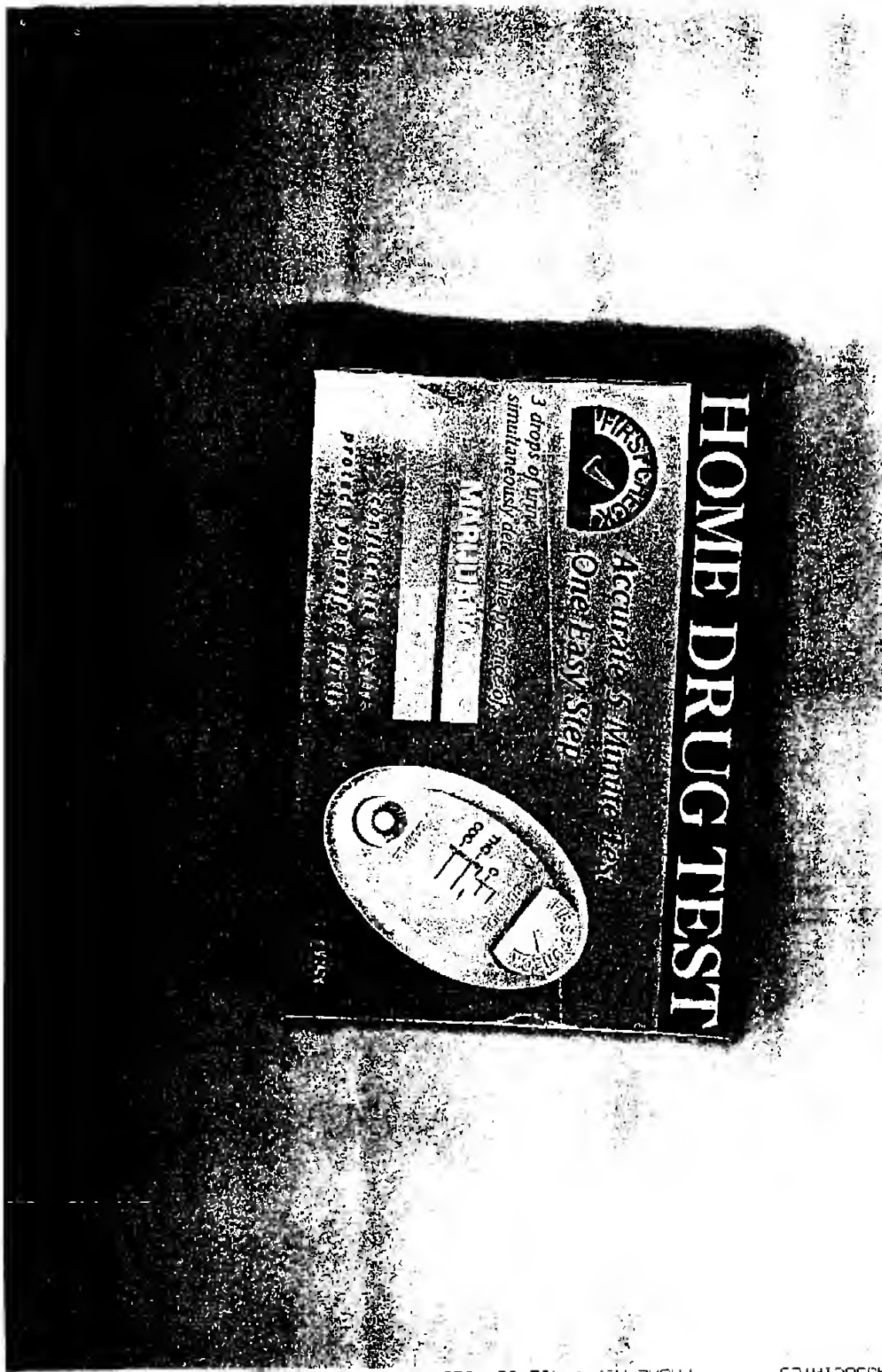
The test detects only the presence of marijuana (THC), morphine/opiates, cocaine, and methamphetamines or their metabolites in urine. A positive test does not provide any information about the amount or level of intoxication.

The test is designed for use with unadulterated urine, only. Adulterants, such as bleach and/or alum, in a urine sample may produce an erroneous result. If adulteration is suspected, the test should be repeated with a new urine sample.

The result must be read 5-10 minutes after sample application. A result read after 10 minutes may not be accurate.

Urine sample should be at room temperature. If sample has been refrigerated, allow sample to reach room temperature before testing.

Certain medications containing opiates or methamphetamines may produce a positive result in any chemical and immunological assay. Additionally, foods and tea containing poppy products and/or coca leaves may produce a positive result. Prolonged exposure to secondhand marijuana smoke may produce a positive result.


HOME DRUG TEST
FIRST CHECK
Accurate 5 Minute Test
One Easy Step
3 drops of urine
simultaneously dee
the presence of
MARIJUANA

For information about other home drug tests call 888-788-5716.
Worldwide Medical Corporation, Irvine, CA 92618 • http://www.wwmed.com

EASY TO TEST

- *Add 3 drops of urine*
- *Wait 5 minutes*
- *Read results*

EASY TO READ RESULTS

First Check® provides immediate information about the use of marijuana and cocaine. It is not for legal, law enforcement, or medical purposes. For diagnosis and treatment, consult with health care or substance abuse professional.

This box contains:
1 test unit
1 sample dispenser
Instructions

Material required but not provided:
Clean glass or plastic container for collection of sample.

For external use only. Store at 40-86°F (4-30°C) Read enclosed directions completely before use.

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[illegible] Marijuana use increased 43% in junior high (grades 6-8) and 28% in high school students (grades 9-12).
National Parents' Resource Institute for Drug Education, Inc. (PRIDE) 9th annual students' survey (September 25, 1996)

In 1995, cocaine related episodes comprised 27% of all emergency department drug related episodes.
1995 Preliminary Estimates of Drug-Related Emergency Department Episodes. SAMHSA/OAS (August, 1996)

The potency of marijuana has doubled since the 1970s.
Marijuana Potency Monitoring Project. Quarterly Report, 1996. Mississippi: University of Mississippi. Research Institute of Pharmaceutical Sciences

Heavy marijuana use is associated with reduced ability to sustain attention, a decreased capacity to shift attention, reduced learning and decreased mental flexibility.
Pope H. and Yurgelun-Todd D. Journal of the American Medical Association. 275: 521-527 (1996)

Among emergency room cocaine-related episodes, "dependence" was the most commonly reported motive for drug use in 1995.
1995 Preliminary Estimates of Drug-Related Emergency Department Episodes. SAMHSA/OAS (August, 1996)

In 1994, when manner of drug abuse death was accidental, cocaine was mentioned in 55% of medical examiner cases.
Statistical Series. Series I, Number 14-B. Drug Abuse Warning Network (DAWN). U.S. Dept. of Health and Human Services

A higher prevalence of depression, motivational problems, and interpersonal problems are associated with marijuana use.
Caron Foundation, Marijuana and Today's Youth (1997)

Educational Materials

Growing Up Drug Free: A Parent's Guide to Prevention, *U.S. Department of Education, Washington, D.C., NCADI Publication No. PHD533, 1993*

Keeping Youth Drug Free: A Guide for Parents, Grandparents ...and Other Caregivers, *Center for Substance Abuse Prevention, U.S. Department of Health and Human Services, 1995*

Marijuana: Facts for Teens, *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD713, 1995*

Marijuana: Facts Parents Need to Know, *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD712, 1995*

Support Groups

Al-Anon Family Group Headquarters
PO Box 862
Midtown Station
New York, NY 10018-0862
800/344-2666

World Service Office, Inc.
P.O. Box 9999
Van Nuys, CA 91409
818/773-9999

Marijuana Anonymous
World Services Office
PO Box 2912
Van Nuys, CA 91404
800/766-6779

Families Anonymous, Inc.
P.O. Box 3475
Culver City, CA 90231-3475
800/736-9805

WORLDWIDE MEDICAL CORPORATION
Irvine, CA 92618 U.S.A.
toll free 888/788-5710
Visit Worldwide Medical Corporation at http://www.wwmed.com

Commonly Asked Questions:

Q: The marijuana test line is lighter than the lines for cocaine or Control. Does this mean some marijuana is present? [illegible]

A: No. The lines need not be the same shade or intensity. The control line may look darker than a test line, or vice versa.

Q: How long will the colored lines remain visible? [illegible]

A: The test should be read within 10 minutes for best results. A negative result (3 lines, 1 line in Control window and 2 lines in Test window) will never disappear.

Q: I am not sure of my test results. What should I do? [illegible]

A: The test is working properly as long as a colored line is visible in the Control window. The result is negative for marijuana and cocaine if there are also 2 lines in the Test window. The result is positive if there is no line next to a drug name in the Test window.

Q: Do I have to wait the full 5 minutes before reading the test? [illegible]

A: Yes, we recommend that you wait the full 5 minutes before reading the result. However, if your test clearly shows negative (3 lines, a line in the Control window and 2 lines in the test window), you do not need to wait. If a line in the test window is not clear, your result will be more accurate after 5 minutes. Most negative test results will be clearly readable in 1 minute. To be sure of a positive (1 line in Control window and no line next to a drug name in the Test window), wait 5 minutes but no longer than 10 minutes.

Q: What if my child refuses to give a urine sample? [illegible]

A: Patiently gain your child's cooperation with the understanding that it is their welfare that you are protecting. Should your child question the importance of testing him or her for marijuana and cocaine or the seriousness of occasional drug usage, page 4 of this pamphlet supplies current data on drug usage among our youth and why you, as a parent, cannot ignore this possibility. Be persistent without accusations, threats, or anger. If your child continues to refuse, seek professional help. Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information and educational resources for more information.

Q: Even though the result is negative, I [illegible] my child may be using drugs. What can I do?

A: Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information.

Q: [illegible]

A: Save the unused portion of the urine sample. Ask your family physician for a recommended laboratory to retest the same sample.

HOME DRUG TEST

Instructions for Use

First Check™ Marijuana & Cocaine

When the need to know is....now

- Simple - one step
- Easy-to read
- Confidential
- Result in 5 minutes

First Check® Marijuana & Cocaine provides immediate information about the use of marijuana and cocaine. It is not for legal, law enforcement, or medical purposes. For diagnosis and treatment, consult with a health care or substance abuse professional.

Read the following directions completely before use.

For external use only.
Store at 36-86°F (2-30°C).

FOR EDUCATIONAL USE ONLY

First Check®
Marijuana & Cocaine

Not to be taken internally.

Fast: Results in 5 minutes

Simple: just one step

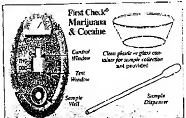
Easy to read: a line or no test line

Accurate: [illegible] accurate in laboratory studies

Marijuana & Cocaine

THC is the primary active ingredient in marijuana (cannabinoids). When ingested or smoked, it produces euphoric effects. Users have impairment of short term memory and marijuana use slows learning. Also, it may cause transient episodes of confusion, anxiety, or even frank toxic delirium. Long term, relatively heavy use may be associated with behavioral disorders. The peak effect of smoking marijuana occurs in 20-30 minutes and the duration is 90-120 minutes after one cigarette. Elevated levels of urinary metabolites are found within hours of exposure and remain detectable for 3-10 days after smoking.

Cocaine derived from the leaves of coca plant is a potent central nervous system (CNS) stimulant and a local anesthetic. Cocaine induces euphoria, confidence and a sense of increased energy in the user; these psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine is used by smoking, intravenous, intranasal or oral administration and excreted in the urine primarily as benzoylecgonine in a short time. Benzoylecgonine has a longer biological half-life (5-6 hours) than cocaine (0.5-1.5 hours) and can generally be detected for 24-60 hours after cocaine use or exposure.



Before you begin

Read all the information in this pamphlet before performing the test. First, make sure you are familiar with the test kit contents shown, below. Store at 36-86° F (2-30° C) in the sealed pouch, away from direct sunlight. Do not use after the expiration date stamped on the package.

Instructions

1. Open the sealed pouch, remove the First Check® card, and set the card on a flat surface with Test and Control windows facing up.
2. Collect urine sample in a clean plastic or glass container.
3. With sample dispenser over sample, press bulb between thumb and index finger, insert dispenser opening into sample and release pressure on bulb. Sample will fill half of dispenser tube.

Do not discard the unused urine until after the test has been completed and the result interpreted.

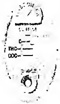
4. With sample dispenser in vertical position over Sample well of test card, gently squeeze dispenser bulb, to allow 3 fully-formed drops of urine, one at a time, to freefall into Sample well.

Do not [illegible] drop [illegible] sample [illegible] Sample well.

5. Allow the test card to remain undisturbed until result is read. Read the result after 5 minutes but within 10 minutes.

Results

Wait at least 5 minutes but not more than 10 minutes before reading result.



Negative

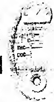
Three horizontal lines, one line in the Control (upper) window and two lines in the Test (lower) window, means there is no marijuana and no cocaine present in the urine sample. *The lines in the Test window may be lighter or darker than the line in the Control window.*

no drug taken.

Positive

One line in the Control window and no line next to a drug name in the Test window means the sample contains that drug.

drug taken (cocaine)



Invalid Test

A distinct colored line should always appear in the Control (upper) window. If no line appears in the Control window, do not interpret result.

Limitations

The First Check® One-Step Home Drug Test is not reusable. The test instructions must be followed precisely.

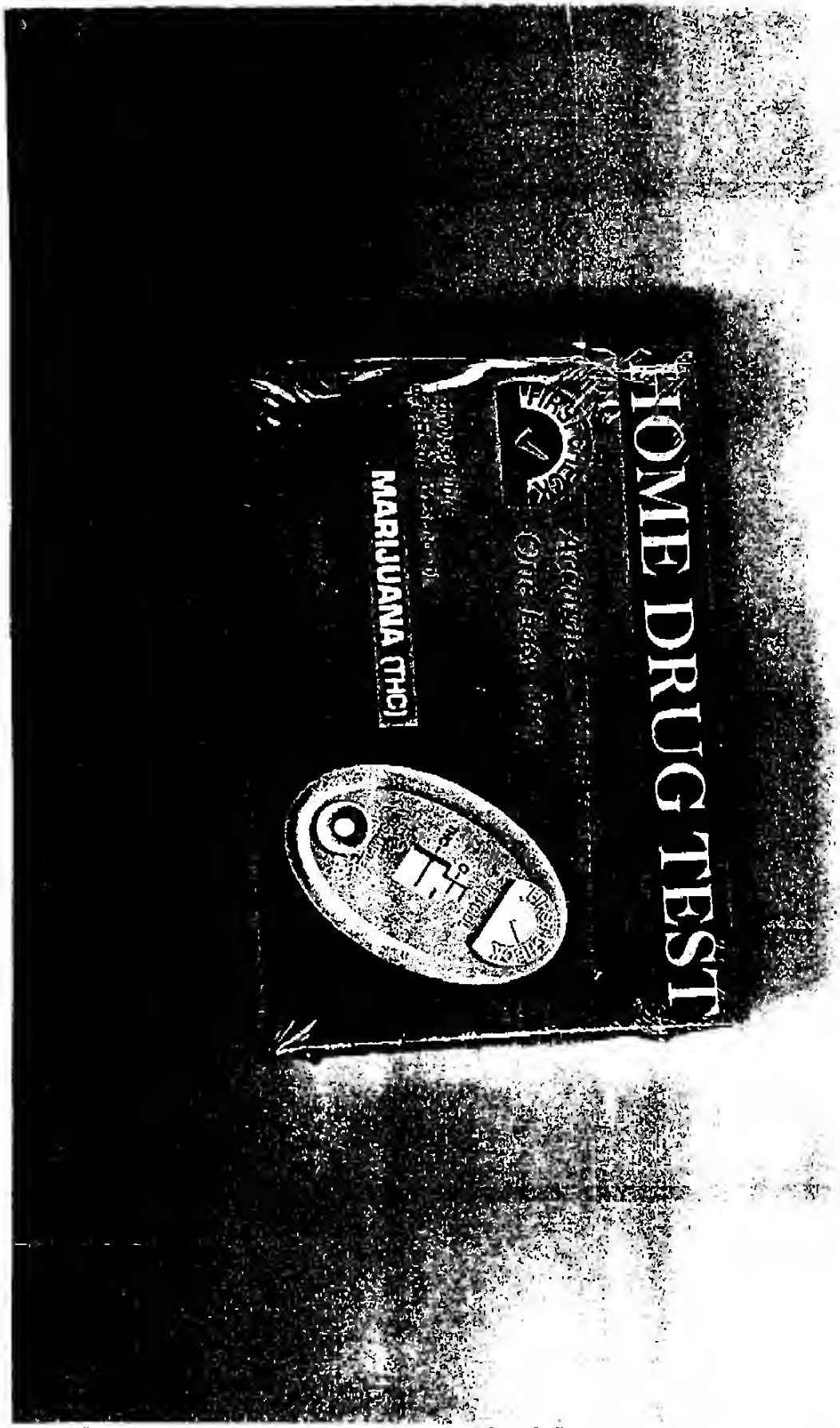
The test detects only the presence of marijuana (THC) and cocaine or their metabolites in urine. A positive test does not provide any information about the amount or level of intoxication.

The test is designed for use with unadulterated urine only. Adulterants, such as bleach and/or alum, in a urine sample may produce an erroneous result. If adulteration is suspected, the test should be repeated with a new urine sample.

The result must be read 5-10 minutes after sample application. A result read after 10 minutes may not be accurate.

Urine sample should be at room temperature. If sample has been refrigerated, allow sample to come to room temperature before testing.

Prolonged exposure to secondhand marijuana smoke may produce a positive result.



For information about other home drug tests call 888-788-5716.
Worldwide Medical Corporation, Irvine, CA 92618 • http://www.wwmed.com

EASY TO TES

- *Add 3 drops of urine*
- *Wait 5 minutes*
- *Read results*

EASY TO READ RESULTS

control line

THC

negative - - -

positive - -

First Check® Marijuana provides immediate information about the use of marijuana. It is not for legal, law enforcement, or medical purposes. For diagnosis and treatment, consult with health care or substance abuse professional.

This box contains:
1 test unit
1 sample dispenser
Instructions

Material required but not provided:
Clean glass or plastic container for collection of sample.

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For external use only. Store at 40-86°F (4-30°C). Read enclosed directions completely before use.

Current Marijuana Trends

Marijuana use increased 43% in junior high (grades 6-8) and 25% in high school students (grades 9-12).
National Parents' Resource Institute for Drug Education, Inc. (PRIDE) 8th annual students' survey (September 25, 1996)

The potency of marijuana has doubled since the 1970s.
Marijuana Potency Monitoring Project Quarterly Report", 1996. Mississippi, University of Mississippi, Research Institute of Pharmaceutical Sciences

Heavy marijuana use is associated with reduced ability to sustain attention, a decreased capacity to shift attention, reduced learning and decreased mental flexibility.
Pope H. and Yurgelun-Todd D., Journal of the American Medical Association, 275, 521-527 (1996)

15% and 25% of boys and girls, respectively, who used marijuana at least 3 times in the last month, are less likely to use condoms than those who never use marijuana.
New York: Columbia University, Center on Addiction and Substance Abuse, (1996, June)

One marijuana cigarette equals twenty regular cigarettes in terms of bronchial damage.
Tashkin D.P. and et al, National Institute on Drugs and Alcohol Research Monograph, 99 (1990)

A higher prevalence of depression, motivational problems, and interpersonal problems are associated with marijuana use.
Canna Foundation, Marijuana and Today's Youth (1997)

Educational Materials

Growing Up Drug Free: A Parent's Guide to Prevention, *U.S. Department of Education, Washington, D.C., NCADI Publication No. PHD533, 1995*

Keeping Youth Drug Free: A Guide for Parents, Grandparents, and Other Caregivers, *Center for Substance Abuse Prevention, U.S. Department of Health and Human Services, 1995*

Marijuana: Facts for Teens, *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD713, 1995*

Marijuana: Facts Parents Need to Know, *National Institute on Drug Abuse, U.S. Department of Health and Human Services, NCADI Publication No. PHD712, 1995*

Support Groups

Al-Anon Family Group Headquarters
P.O. Box 862
Midtown Station
New York, NY 10018-0862
800/344-2666

Marijuana Anonymous
World Services Office
P.O. Box 2912
Van Nuys, CA 91404
800/766-6779

Families Anonymous, Inc.
P.O. Box 3475
Culver City, CA 90231-3475
800/736-9805

Commonly Asked Questions:

Q: The test line is lighter than the line in the Control window. Does this mean some marijuana is present?

A: No. Both lines need not be the same shade or intensity. The control line may look darker than the test line, or vice versa.

Q: How long will the colored line remain visible?

A: The test should be read within 10 minutes for best results. A negative result (2 lines, 1 line in Control window and 1 line in Test window) will never disappear.

Q: I am not sure of my test result. What should I do?

A: The test is working properly as long as a colored line is visible in the Control window. The result is negative for marijuana if there is also a line in the Test window. The result is positive if there is no line in the Test window.

Q: Do I have to wait the full 3 minutes before reading the test?

A: Yes, we recommend that you wait the full 3 minutes before reading the result. However, if your test clearly shows negative (2 lines, a line in both the control and test windows), you do not need to wait. If the line in the test window is not clear, your result will be more accurate after 3 minutes. Most negative test results will be clearly readable in 1 minute. To be sure of a positive (1 line in Control window and no line in Test window), wait 3 minutes but no longer than 10 minutes.

Q: What if my child refuses to give a urine sample?

A: Patiently gain your child's cooperation with the understanding that it is their welfare that you are protecting. Should your child question the importance of testing him or her for marijuana or the seriousness of occasional marijuana usage, page 4 of this pamphlet supplies current data on marijuana usage among our youth and why you, as a parent, cannot ignore this possibility. Be persistent without accusations, threats, or anger. If your child continues to refuse, seek professional help. Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information and educational resources for more information.

Q: Even though the result is negative, I still feel that my child may be using drugs. What can I do?

A: Check with your physician, your phone directory also provides sources of assistance under "Alcohol and Drug Abuse" in the Government and Community Services listings, or page 4 of this pamphlet for Support Group information.

Q: Even though the result is positive, my child claims to be not using drugs. What can I do?

A: Save the unused portion of the urine sample. Ask your family physician for a recommended laboratory to retest the same sample.

HOME DRUG TEST

Instructions for Use

First Check® *Marijuana (THC)*

When the need to know is....now

- Simple - one step
- Easy-to-read
- Confidential
- Result in 3 minutes

First Check® Marijuana provides unsurpassed information about the use of marijuana. It is not for law enforcement, or medical purposes. For detection & treatment, consult with a health care or substance abuse professional.

Read the following directions completely before use.

For external use only.

Store at 36-86°F (2-30°C).

FOR EDUCATIONAL USE ONLY

First Check®
Marijuana (THC)

Not to be taken internally.

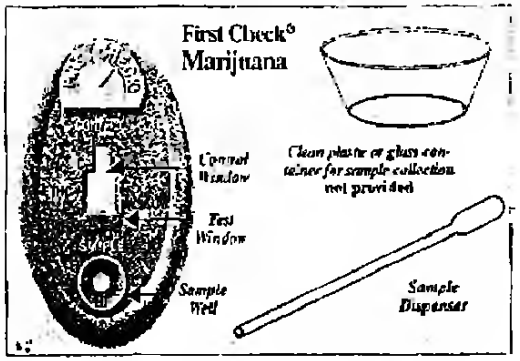
Fast. Results in 3 minutes.
Simple. Just one step.
Easy-to-read. Test line or no test line.
Accurate. Over 99% accurate in laboratory studies.

Marijuana (THC)

THC is the primary active ingredient in marijuana (cannabinoids). When ingested or smoked, it produces euphoric effects. Users have impairment of short term memory and marijuana use slows learning. Also, it may cause transient episodes of confusion, anxiety, or even frank toxic delirium. Long term, relatively heavy use may be associated with behavioral disorders. The peak effect of smoking marijuana occurs in 20-30 minutes and the duration is 90-120 minutes after one cigarette. Elevated levels of urinary metabolites are found within hours of exposure and remain detectable for 3-10 days after smoking.

Before you begin

Read all the information in this pamphlet before per-forming the test. First, make sure you are familia with the test kit contents shown, below. Store at 36-86° F



2-30° C) in the sealed pouch, away from direct sunlight Do not use after the expiration date stamped on the package.

Instructions

1. Open the sealed pouch, remove the First Check® card, and set the card on a flat surface with Test and Control windows facing up.
2. Collect urine sample in a clean plastic or glass container.

3. With sample dispenser over sample, press bulb between thumb and index finger insert dispenser opening into sample and release pressure on bulb. You should see sample fill half of dispenser tube.

Do not discard the unused urine until after the test has been completed and the result interpreted.

4. With sample dispenser in vertical position over Sample well of test card, gently squeeze dispenser bulb, to allow 3 fully-formed drops of urine, one at a time, to free-fall into Sample well.

Do not "touch-off" drops. If flow of sample is not seen in the Test window, add 1 more drop of urine to Sample well.

5. Allow the test card to remain undisturbed until result is read. Read the result after 3 minutes but within 10 minutes.

Results

Wait at least 3 minutes but not more than 10 minutes before reading result.

2 lines - negative
Two horizontal lines, one in each of the Control (upper) window and Test (lower) window, means there is no marijuana present in the urine sample. *The line in the Test window may be lighter or darker than the line in the Control window.*

no drug taken

1 line - positive
One line in the Control window and no line in the Test window means the sample contains marijuana.

drug taken

Invalid Test
A distinct colored line should always appear in the Control (upper) window. If no line appears in the Control window, do not interpret result.

Limitations

The First Check® One-Step Home Drug Test is not re usable. The test instructions must be followed precisely.

The test detects only the presence of marijuana (THC) or its metabolites in urine. A positive test (no line in Test window) does not provide any information about the amount or level of intoxication.

The test is designed for use with unadulterated urine, only. Adulterants, such as bleach and/or alum, in a urine sample may produce an erroneous result. If adulteration is suspected, the test should be repeated with a new urine sample.

The result must be read 3-10 minutes after sample application. A result read after 10 minutes may not be accurate.

Urine sample should be at room temperature. If sample has been refrigerated, allow sample to come to room temperature before testing.

Prolonged exposure to secondhand marijuana smoke may produce a positive result.